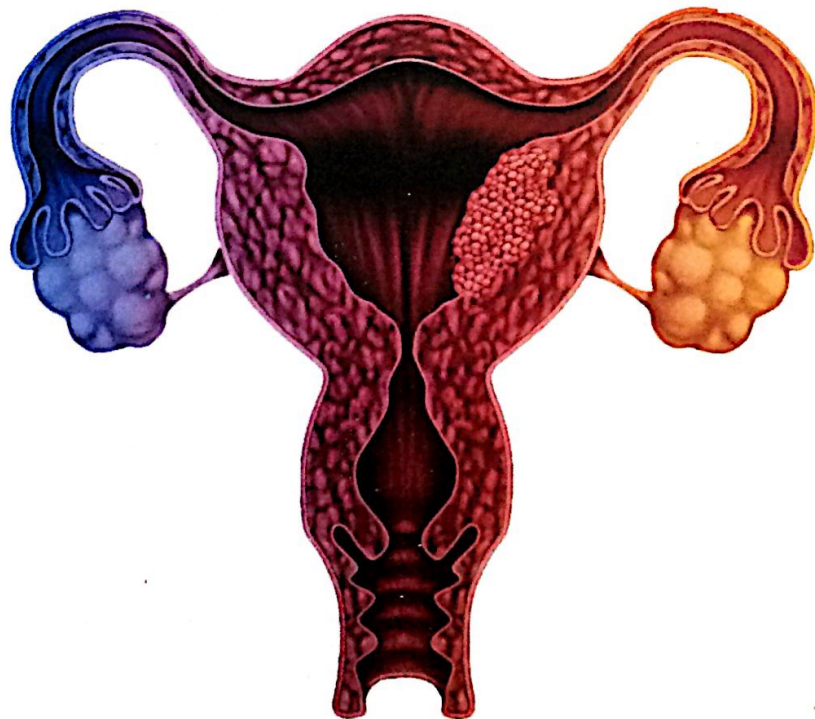


Easy Pathology

— Dr. Abdelrahman Khalifa —

Female & Breast

Part 2



Ain Shams 2017 - 2018

VISIT...

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Breast carcinoma

Incidence: Females : males 125:1 (carcinoma in females has worse prognosis, ductal type)

P.F.:

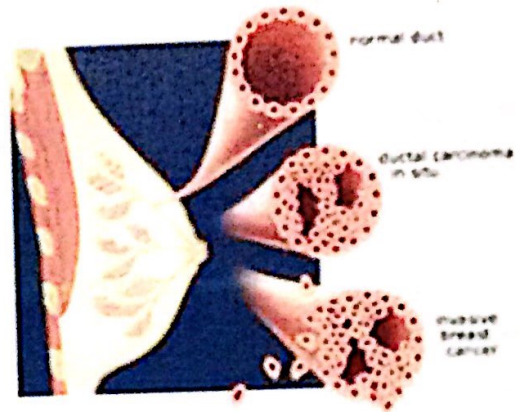
- Genetic (e.g. **BRCA** gene mutation), more in European & north Americans
- Family history (up to 3 times increased risk)
- Age >50 y (only 5 % below 40y)
- Excess & prolonged **estrogen** effect (early menarche <12y & late menopause >55)
- **Nullipara, non-lactating** females
- Obesity
- Others: *Radiation, Smoking, Alcohol*

P.L.:

- Atypical Mammary hyperplasia (>2 folds)
- Carcinoma insitu (LCIS up to 12 folds)

Pathogenesis: cause is Unknown

- **Genetic** :
 - **HER2/NEU** → proto-oncogene → Aggressive tumor
 - **BRCA1** or 2 mutation (Tumor suppressor) in 5-10%
- **Hormonal** : **Estrogen** after menopause (?) → production of **G.F.** by epithelial cells
- **Environmental**: Radiation & Diet



Types:

- **Ductal** (the most common)
 - Duct carcinoma insitu (**DCIS**)
 - Invasive duct carcinoma (**IDC**)
 - **'Scirrhous'**, not otherwise specified (IDC-NOS) >70%
 - **Mucoid carcinoma** (Colloid)
 - **Medullary carcinoma** 1%
 - **Tubular** 10%
 - **Paget disease**
 - **Inflammatory carcinoma**
- **Lobular**
 - Lobular carcinoma insitu (**LCIS**)
 - Invasive lobular carcinoma (**ILC**)

Duct carcinoma insitu (DCIS)

Micro: Large Atypical cells inside the duct. **BM is intact**. May show calcification

Papillary: forming papillary projection inside the duct

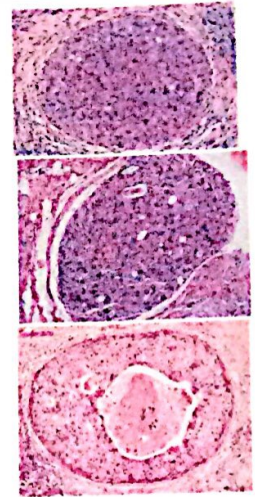
Solid: duct is filled with malignant cells

Crebriform: similar to solid but has multiple lumens

Comedo: showing central necrosis (acidophilic debris)

Mostly DCIS is mixed

Prognosis & fate: **Excellent** prognosis with early detection. 30 % become invasive with time.



Scirrhous carcinoma IDC -NOS

Gross:

Skin: retracted nipple – Lymphedema – dimpling (peau d' orange)

Site: Upper lateral quadrant

Shape: Irregular ill-defined

Consistency: Firm-Hard (scirrhous) & fixed

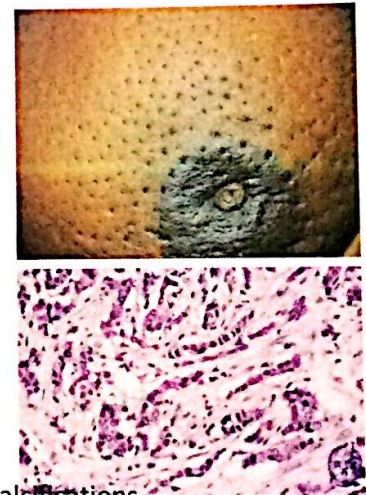
C/S: Gritty & grayish white

Micro:

Malignant cells: solid sheets or tubules of malignant cells + micro calcifications

Stroma: Extensive fibrous desmoplastic reaction

Prognosis & immunophenotyping: (60% hormonal dependant. **30% HER2/NEU**)

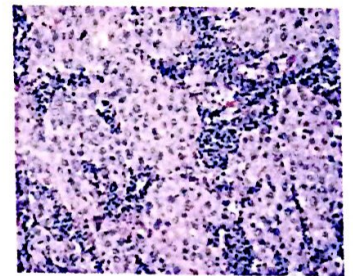


Medullary carcinoma (associated with **BRCA-1**)

Gross: well defined, Soft.

Micro: Solid sheets of large anaplastic cells (**Cellular**) + **lymphocytic** infiltration
little stroma - **Pushing borders**

Prognosis: relatively good (**No HER2/NEU**. But No hormonal dependence)

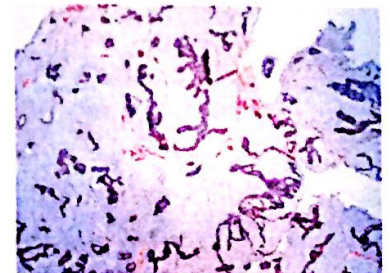


Mucoid (colloid) carcinoma

Gross: well-defined, Soft gelatinous mass

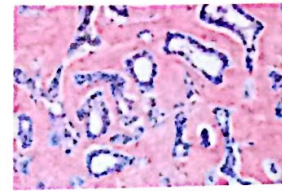
Micro: mucous secreting malignant cells + **mucin lakes**

Prognosis: relatively good (**No HER2/NEU**. **hormonal dependant**)



Tubular carcinoma 10%

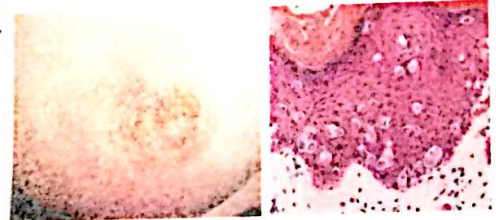
The tumor is **small <1cm** forming tubular structures.
Prognosis is good (**No HER2/NEU**, **hormonal dependant**)

**Paget's disease of the breast**

Gross: Thick, crusted, **red nipple** & areola → ulcerated

Micro: Large atypical **clear cells** in the base of epidermis
+ **DCIS** or **invasive carcinoma** of the breast

Prognosis: According to the type of carcinoma. Bad in case of misdiagnosis

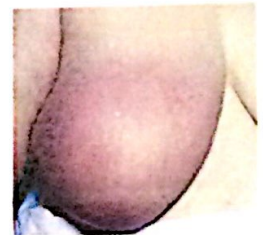
**Inflammatory carcinoma**

(*carcinoma mimics inflammation*)

Gross: **non palpable** mass, masked by **Red swollen** breast (Peaud' orange is common)

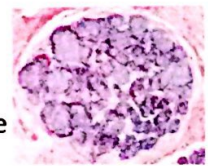
Micro: poorly differentiated cells + **vascular emboli** + massive **lymphatic infiltration**

Prognosis: Bad prognosis

**Lobular carcinoma insitu (LCIS)**

Micro: **small monotonous** cells inside lobules, **mucinous** changes are seen. **BM** is intact

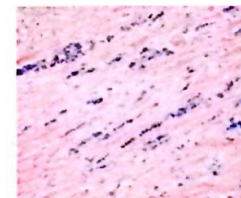
Prognosis: accidentally discovered, with increased risk of **bilatrality** & **multifocality**. Became invasive in 30%.

**Invasive lobular carcinoma (ILC)**

Gross: irregular firm masses. Bilateral, multifocal

Micro: small malignant cells arranged in lines (**Indian files**) + fibrous stroma
In some cases they **arrange around acini or ducts**, giving **Bull's eye**, or **Target** appearance

Prognosis: good (**No HER2/NEU**, **& hormonal dependant**)

**C/P & Complications of cancer breast:**

- Painless mass (palpable or by mammogram)
- Skin Signs (??)
- **Spread:**
 - Direct → Skin, muscle, ribs
 - Lymphatic:
 - Permeation → lymphedema of breast, arm
 - Lymphatic embolism → axillary LN & internal mammary LNs
 - Blood: Lung – Bone – **Adrenals** – Liver – Brain, rarely spleen, ovary, & pituitary

Prognostic factors:

- **Sex:** cancer in males → worse prognosis
- **Age:** very Young & very Old age → worse prognosis
- **Microscopic** type (??)
- **Stage** (Size of tumor – LN metastasis – blood spread)
- **Grade** (Less tubular structure, More mitoses & necrosis) → worse prognosis
- **Hormonal** dependence (**Er, Pr** receptors) → better prognosis
- **Genetic** typing (**her2/neu** gene expression → bad prognosis)
- **Proliferative** rate (detected by **Ki67**) → worse prognosis

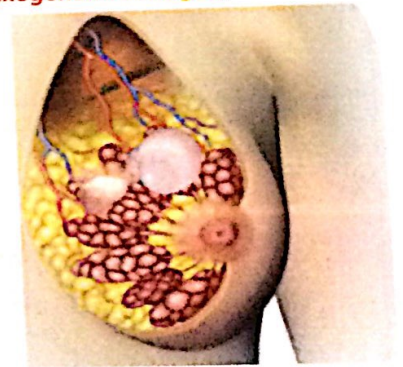
Fibrocystic disease (Mammary cystic hyperplasia)

Incidence: the most common breast disease middle aged females

P.F.: Cyclic breast changes during menstrual cycle. (*Not related to exogenous estrogen*)

Gross:

- **Site:** Bilateral, multifocal
- **Shape:** ill defined
- **Consistency:** firm
- **C/S:** cysts (1-5 cm) containing fluid (Blue or brown cysts)

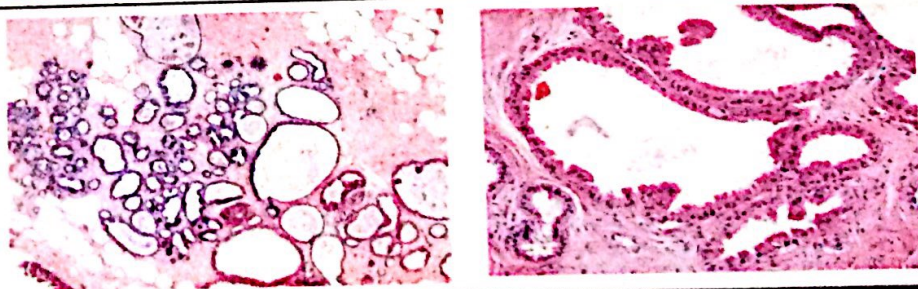
Micro:

- **Adenosis** : proliferated acini
- **Fibrosis**
- **Sclerosing adenosis**: excess fibrosis + obliterated acini & ducts (*mistaken as carcinoma*)
- **Epitheliosis** : Hyperplasia of lining epithelium of both acini and ducts + papillomatosis and **atypia** in duct epithelium (*precancerous*)
- **Cystic dilatation** of ducts with **apocrine metaplasia** (*Large granular eosinophilic cells*)

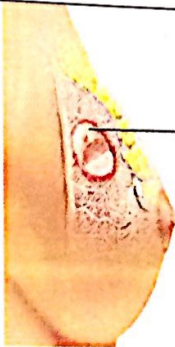
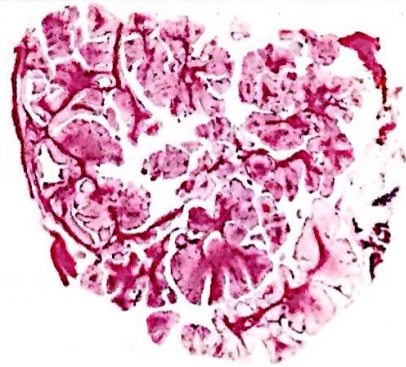
Complications:

Hyperplasia , Papillomatosis, Sclerosing adenosis → Low risk of Carcinoma

Atypical hyperplasia → High risk of carcinoma (5 folds)



Benign tumors

	Fibro adenoma	Phyllodes	Duct papilloma
Incidence	The most common tumor of breast Young - estrogen	Less common Older 45 y	Less common
Gross	Rounded – less than 10 cm – capsulated – freely movable – grayish white	Similar but : Larger 1-45 cm Cut section: cystic spaces with leaf-like papillary projections	Small mass
	 Fibroadenoma		
Micro	Pericanalicular : patent ducts + fibroblastic stroma Intracanalicular : obliterated ducts + excess stroma All ducts are lined by cuboidal epithelium + myoepithelial cells	cystic spaces and leaf-like projections + excess cellular stroma (malignant changes : Increased stromal cellularity + Anaplasia & mitoses+ invasion)	Branched papilloma with Columnar & myoepithelial cells
			
Fate	No malignant trans Regress after menopause	Benign, or malignant	Bleeding per nipple

Inflammatory lesions

• Traumatic fat necrosis

- Firm/Hard calcified mass
- Following trauma of the breast → fat necrosis → calcifications
- Necrotic fat cells + pale macrophage & giant cells + fibrosis & calcification
- Mistaken as carcinoma



• Suppurative mastitis

- Pyogenic infection in lactating females (enters through nipple fissures)
- Abscess → heal by fibrosis → firm mass with retracted skin

• Duct-ectasia (plasma cell mastitis)



- Old females
- Accumulated secretions → Inflamed dilated ducts → ruptured ducts → granuloma & fibrosis
- Inflammatory cells are lymphocytes & plasma cells

Gynecomastia:

enlarged male breast. Excess estrogen (Liver failure – Klinefelter – puberty – Old)
Button-like, **retroareolar mass**.

Micro: Proliferated **duct hyperplasia** + **hyalinosis** of stroma



Acute salpingitis

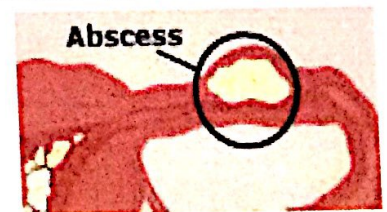
Suppurative inflammation of tubes. (**Gonococci**, IUD). Tubes are swollen containing pus

Chronic salpingitis

Following acute → Fibrosis & adhesions + chronic inflammatory cells

T.B. salpingitis

2ry (**Blood** or **lymphatics** from Intestine). Morphology: caseating granulomas (describe)



Complications of salpingitis:

Peritonitis – Tuboovarian abscess – Sterility – **Tubal pregnancy**

Tubal pregnancy

Congenital diseases of tube - Chronic **salpingitis** – **Endometriosis**
 Distended with hemorrhagic clot & chorionic villi → **abortion** – peritoneal bleeding



Tumors of the tubes: **rare**. Adenocarcinoma – Fibroma - Leiomyoma

Tubo-ovarian abscess

Suppurative inflammation of tubes leading to destruction & adhesion with ovaries

Morphology: Irregular mass. Wall is fibrotic. Lumen contains pus

Chronic Granulomatous Oophoritis: TB or Bilharziasis (rare)

Abnormal female genital tract bleeding

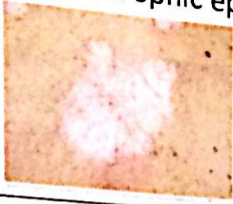
Menorrhagia: Excessive blood during period **Metrorrhagia:** Abnormal bleeding **between** menstrual phases

- **General** e.g. Blood diseases, Leukemia
- **Local :**
 - **Pre-puberty :**
 - **Precocious puberty**
 - Tumor (Sarcoma **Botryoides**)
 - **Adult:**
 - Dysfunctional bleeding
 - **Endometrial hyperplasia**
 - Polyps
 - Tumors (e.g. **leiomyoma**, carcinoma)
 - **Menopause :**
 - **Dysfunctional**
 - Endometrial hyperplasia
 - Polyps
 - Tumors (**Carcinoma**)
 - **Pregnant:**
 - complications of pregnancy - **Abortion** - ectopic pregnancy
 - Tumors(**Trophoblastic**, Leiomyoma)

Causes of Vulvitis: same causes of **Cervicitis** (?)

Bartholin Cyst of vagina : similar to nabothian cyst of the cervix (?)

Vulvar Dystrophy (Leukoplakia)

Lichen sclerosus	Lichen simplex chronicus
Skin fibrosis → Atrophic epithelium	Hyperplasia & <u>chronic</u> inflammation
	
Precancerous	More precancerous

Condyloma acuminata	Condyloma Lata
Caused by HPV 6,11 (not precancerous)	Caused by 2ry Syphilis
Papillary bulky lesion	Falt lesion
	
Branched Squamous cell papilloma + koilocytosis	Hyperplastic skin + syphilitic lesion

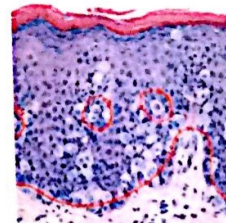
VIN : I, II, III similar to **CIN** (?) → progress to Carcinoma of the vulva (Sq.C.C similar to cervical carcinoma.)

Paget disease of the vulva

Gross: **Red**, demarcated, **crusted** lesion in labia major

Micro: Large vacuolated cells within epidermis (**paget cells**)

Fate: **Precancerous** → Invasive after many years

**Diseases of Vagina**

Congenital.: Absence – Septate double vagina – Lateral Vaginal cyst (Gartner cyst)

Vaginitis.: **Bacterial** vaginitis by commensal bacilli – **Candidiasis** 'monilia' – **Trichomonas** 'green discharge')

Tumors of vagina:

- Squamous cell carcinoma
- Clear cell adenocarcinoma: in Daughters of Mothers used **DES**
- **Embryonal Rhabdomyosarcoma** (*Botryoides sarcoma*)
Grape-Like red papillary mass Age: <6 y

1) *Peau d'orange* appearance of the mammary skin in case of breast carcinoma is due to:

- a. Large size of the tumor
- b. Hard consistency of the tumor
- c. Infiltration of dermal lymphatics
- d. Inflammation of the covering skin

2) A 42-year-old woman had a 9 cm, soft and fleshy, movable mass in her left breast. The overlying skin was normal and there was no axillary lymphadenopathy. Microscopically the mass composed of sheets of large cells with pleomorphic nuclei and indistinct cell borders. The stroma show heavy lymphoplasmacytic infiltrate. Which of the following is the most likely diagnosis?

- a. Lobular carcinoma
- b. Paget's disease of the breast
- c. Invasive duct carcinoma
- d. Medullary carcinoma
- e. Phylloids Tumor

3) A 50 year old woman with history of recent trauma to the left breast presented with a hard nodule. Excisional biopsy was done and sections revealed necrotic fat cells infiltrated by foamy histocytes. Which of the following is the most likely diagnosis ?

- a. Sclerosing adenoma
- b. Fat necrosis
- c. Mammary duct ectasis
- d. Fibrocystic changes
- e. Mastitis

4) Choriocarcinoma consists of all except:

- a. Malignant cyto and syncytiotrophoblast
- b. Areas of haemorrhage and necrosis
- c. Malignant cells invading uterine wall
- d. Fibrous stroma

5) Schiller-Duval bodies are characteristic of :

- a. Teratoma
- b. Dysgerminoma
- c. Endodermal sinus tumor
- d. Choriocarcinoma
- e. Embryonal carcinoma

6) The chocolate ovarian cyst refers to :

- a. Follicular cyst
- b. Theca lutein cyst
- c. Neoplastic cyst
- d. Endometriotic cyst
- e. All of the above

7) Adenomyosis is:

- a. Closely related to leiomyoma
- b. Closely related to endometrial hyperplasia
- c. a type of endometriosis
- d. a tumor like lesion
- e. a precancerous lesion

8) Features of puerperal sepsis include all except:

- a. acute suppurative inflammation
- b. caused by streptococcus haemolysis
- c. follow labour or abortion
- d. uterus is atrophic and firm
- e. the endometrium is infiltrated by many polymorphs

9) Female patient presented with reddish swelling at the site of abdominal scar which monthly becomes painful and tender. Which of the following is the most likely diagnosis?

- a. Kertinous cyst
- b. Endometriosis
- c. Abscess
- d. Intradermal naevus

10) A 36-year-old woman has had episoides of lower abdominal pain for the past 10 years. Laparoscopy revealed multiple slightly raised brown lesions measuring 0.2 to 0.5 cm. located over the serosal surface of the uterus, fallopian tube and appendix. Which of the following microscopic findings is most likely present in these lesions.

- a. Endometrial glands and stroma
- b. Mesothelioma
- c. Metastatic carcinoma
- d. Caseating granulomas

11) A 23-year-old woman with amenorrhea, went to the emergency room because of sudden onset of lower abdominal pain. A transvaginal U/S showed no intrauterine gestational sac, Which of the following is most useful procedures to perform at this point for the patient?

- a. WBC count
- b. Urine analysis with microscopic examination
- c. Pap smear
- d. Serum beta-HCG
- e. Endometrial biopsy

12) A 38-year-old woman had a cervical biopsy showing dysplasia involving the full thickness of the cervical epithelium. Which of the following is the most likely diagnosis?

- a. Cervical intraepithelial neoplasia III
- b. Endocervical adenocarcinoma
- c. Extramammary paget's disease
- d. Severe chronic cervicitis
- e. previous estrogen exposure

13) A 65-year-old woman presented with pruritic red, crusted, sharply demarcated map-lesion involving a large portion of her labia majora. Histologic examination revealed large, vacuolated anaplastic tumor cells, infiltrating the epidermis, singly and in clusters. Which of the following is the most likely diagnosis?

- a. Clear cell adenocarcinoma
- b. Malignant melanoma
- c. Extramammary paget's disease
- d. Sarcoma botryoids
- e. Squamous cell carcinoma

14) A 59-year-old postmenopausal woman suffered from bleeding which has been present for a couple of months. Endometrial biopsy was done for her and revealed atypical hyperplasia. This lesion most likely resulted from

- a. HPV infection
- b. Unopposed estrogenic stimulation
- c. Pelvic inflammatory disease
- d. Long term oral contraceptive pills
- e. Chronic endometritis

15) A 23-year-old woman presented with pelvic pain, and was found to have a left ovarian mass. The mass measured 3 cm, and the cut section was cystic filled with straw-colored fluid. Histologically the cyst was lined by tall columnar cells with some ciliated cells. Which of the following is the most likely diagnosis?

- a. Mucinous tumor
- b. Endometrioid tumor
- c. Clear cell tumor
- d. Brenner tumor
- e. serous tumor

Match

- | | |
|--------------------------------------|--|
| 1- Medullary carcinoma of the breast | a) Leaf like projections |
| 2- Paget's disease of the breast | b) Grape like mass |
| 3- Invasive lobular carcinoma | c) Syphilitic reaction |
| 4- Fibrocystic disease | d) Foreign body giant cells |
| 5- Fibroadenoma | e) Intraductal necrosis |
| 6- Phyllodes tumor | f) Scanty stroma rich in lymphocytes |
| 7- Sarcoma botryoides | g) Large vacuolated cells in epidermis |
| 8- Condyloma latum | h) Indian files pattern |
| 9- Traumatic fat necrosis | i) Sclerosing adenosis |
| 10- Comedo carcinoma | j) Biphasic tumor |

Enumerate

- 1- Different locations of Paget Diseases ?
- 2- Causes of breast lump in young non-lactating woman ?
- 3- Microscopic findings of Fibrocystic disease ?
- 4- Tumor markers of ovarian tumors?
- 5- Sites of choriocarcinoma?
- 6- Types of invasive duct carcinoma ?
- 7- Causes of Gynecomastia?
- 8- Prognostic factors of breast carcinoma?

44. A 65 -year- old woman presents with a pruritic red, crusted, sharply demarcated map-lesion involving a large portion of her labia majora. Histologic sections reveal large, vacuolated anaplastic tumor cells, infiltrating the epidermis, singly and in clusters. These malignant cells stain positively for mucin. Which of the following is the most likely diagnosis?

- a. Clear cell adenocarcinoma
- b. Malignant melanoma
- c. Extramammary Paget's disease
- d. Sarcoma botryoides
- e. Squamous cell carcinoma

46. A 60 year-old postmenopausal woman presents with new onset of uterine bleeding. An endometrial biopsy reveals the presence of crowded, back to back glands. Lining epithelium is stratified, mitotically active with atypical nuclei. Which of the following is the most likely diagnosis?

- a. Simple hyperplasia
- b. Complex hyperplasia
- c. Endometrial carcinoma
- d. Endometriosis
- e. Atypical hyperplasia

47. Prolonged unopposed estrogen stimulation in an adult woman increases the risk of development of endometrial hyperplasia and subsequent carcinoma. Which of the following is the most common histologic appearance of this type of cancer?

- a. Adenocarcinoma
- b. Clear cell carcinoma
- c. Small cell carcinoma
- d. Squamous cell carcinoma
- e. Transitional cell carcinoma

48. A 46-year- old woman undergoes an abdominal hysterectomy for a fibroid uterus. The surgeon requests a frozen section on the tumor which is very difficult because of the high cellularity of the tumor. Which of the following criteria will be used by the pathologist in determining benignancy versus malignancy in permanent sections (paraffin sections)

- a. Mitotic rate
- b. Cell pleomorphism
- c. Cell necrosis
- d. Nuclear cytoplasmic ratio
- e. Tumor size

49. A 25-year-old woman presents with lower abdominal pain, fever, and vaginal discharge. Pelvic examination reveals bilateral adnexal tenderness and pain when the cervix is manipulated. Cultures taken from the vaginal discharge reveals *Neisseria gonorrhoeae*. Which of the following is the most likely cause of this patient's adnexal pain?

- a. Ectopic pregnancy
- b. Endometriosis
- c. Pelvic inflammatory disease
- d. Endometrial hyperplasia
- e. Tuberculous salpingitis

50. A 23-year-old woman presents with pelvic pain and is found to have an ovarian mass of the left ovary, measuring 3 cm. in diameter. Grossly, the mass consists of multiple cystic spaces. Histologically, these cysts are lined by tall columnar epithelium with some of the cells being ciliated. Which of the following is the correct diagnosis for this ovarian tumor which histologically recapitulates the histology of the fallopian tube?

- a. Serous tumor
- b. Mucinous tumor
- c. Endometrioid tumor
- d. Clear cell tumor
- e. Brenner tumor

51. An 18-year-old girl had a large ovarian tumor. On examination, the tumor was solid, rubbery, with nodular surface and grayish-white cut surface. Sections examined reveal a tumour tissue composed of a vacuolated network, containing microcysts, lined by flattened cells, with perivascular substances is most likely to be elevated?

- a. Oestrogen
- b. Androgen
- c. Thyroxin
- d. Alfa fetoprotein
- e. Human chorionic gonadotrophin

52. A 57-year-old woman has recently noticed multicentric, raised, mucosal erythematous areas on the labia. Biopsy specimens from such areas reveal dysplastic cells that occupied about half of the thickness of the squamous epithelium. Which of the following is the most likely diagnosis?

- a. Vulvar chancre
- b. Paget's disease of the vulva
- c. Condyloma acuminatum
- d. Chronic nonspecific vulvitis
- e. Vulvar intraepithelial neoplasia